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Clinical Trials: The Conflict between the Doctors' Financial Interests of In Recruiting Patients and the Patients' Best Interests in Malaysia

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Abstract

The Hippocratic and the principle of beneficence require that doctors should always act in the patient's best interest. However, once the 'doctor' puts on the hat of a 'doctor-investigator' by involving in clinical trials, the responsibility to safeguard the interests of the patient is no longer a priority. This is because the interest or intent of the doctor-investigator is different from that of the doctor who offers medical treatment solely in the best interests of patients. Instead, there are many interests of doctor-investigators, which include financial incentives in return for recruiting patients as research subjects. When there is a conflict between the financial interests of doctors in recruiting patients and patients' best interests, ethical challenges to the integrity of doctor-investigators may arise in making decision which is not bias. Hence, the objective of this paper is to discuss about conflict of interests between the doctor-investigator incentives to recruit and the doctor-investigator's duty to keep the patients' best interest. A qualitative methodology has been used in the process of writing this conceptual paper. The findings show that incentives gained by doctor-investigators in return for recruiting patients violate the principle of ethics because of the conflict of interests bearing in mind that the Hippocratic and the principle of beneficence require doctors to act in the patients' best interest.

Keywords: conflict of interests; incentives, recruiting patients; patients' best interests; drug company; doctor-investigators.

1. Introduction

The Hippocratic and the principle of beneficence require that doctors should always act in the patient's best interest. However, once the 'doctor' puts on the hat of a 'doctor-investigator' by involving in clinical trials the responsibility to safeguard the interests of the patient is no longer a priority. This is because the interest or intent of the doctor-investigator is different from that of the doctor who offers medical treatment solely in the best interests of patients. Instead, there are many interests of doctor-investigators, which include financial incentives in return for recruiting patients as research subjects (Lenrow, 2006).

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It is pertinent to note from the very beginning that recruiting humans as research subjects is important in clinical trials for the development of medical science. Unless an adequate number of participants is entered, the trial will not be able to answer the questions about benefit and risk. Therefore, there is a great pressure to recruit an adequate number of participants and to do so as quickly as possible. Likewise, the process to recruit humans as research subjects is not an easy thing. It is a problem often faced by the drug company wishing to test new drugs. In 2001, the Centre Watch reported that more than 85% of completed clinical trials experienced delay in the recruitment process, while 34% were also delayed for more than a month (Smith, 2008). As such, drug companies are 'forced' to make doctors their target for patient recruitment as research subjects. In return, the doctor-investigators are given incentives for each patient they successfully recruit (Gatter, 2006). When these doctor-investigators are also a patient's doctor, there is a direct conflict of interest between the doctor-investigator's incentives to recruit and the doctor-investigator's duty to keep the patient's best interest in mind (Sandhya Srinivasan, 2010). Where there is a conflict of interest, ethical challenges to the integrity of doctor-investigators will arise.

Conflict of interest in clinical trial may exist when a doctor accepts a fee, gift or other incentive for finding and recruiting research subjects, especially if the research subject is his or her patient (College of Physicians and Surgeons of British Columbia, 2009). Some have defined conflict of interest as a situation in which the self-interest of the individual is in conflict with an obligation (Khushf & Gifford, 1998). Thompson (1993) has defined a conflict of interest as situations that cause conflicts when a decision is made to give priority to the acquisition of secondary importance such as financial income overcome such primary importance welfare of patients. Therefore, it can be said that a conflict of interest generally occurs when a person is entrusted to act or make decisions on behalf of others. In clinical trials, conflict of interest cannot be avoided as doctor-investigators are the one who is responsible to determine whether patients should participate in clinical trials as research subjects (Lo et al, 2000). The Hippocratic and the principle of beneficence require that doctors should always act in the patient's best interest. However, when there is a conflict between the financial interests of the doctor-investigators in recruiting patients and patients' best interests, ethical challenges to the integrity of doctor-investigators may arise in making decision when these doctor-investigators are also a patient's doctor. Hence, the objective of this paper is to discuss about conflict of interest between the doctor-investigator's incentives to recruit and duty to keep the patient's best interest. A qualitative methodology has been used in the process of writing of this conceptual paper.

1.3 The Causes of Conflict of Interests

In general, medical codes of ethics across the world prohibit doctors to put their financial interests above the interests of their patients. For example, the American Medical Association's Code of Medical Ethics specifies that: "Under no circumstances may physicians place their own financial interest above the welfare of their patients". In Malaysia, the Code of Professional

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Conduct adopted by the Malaysia Medical Council states that: "A prescribing practitioner should not only choose but also be seen to be choosing the drug or appliance which, in his independent professional judgment, and having due regard to economy, will best serve the medical interests of his patient. Practitioners should therefore avoid accepting any pecuniary or material inducement which might compromise, or be regarded by others as likely to compromise, the independent exercise of their professional judgment in prescribing matters. … It is improper for an individual practitioner to accept from a pharmaceutical firm monetary gifts or loans or expensive items of equipment for his personal use". However, when it comes to rewards particularly in the form of 'generous money', anyone including doctor-investigators will deviate from these codes of ethics.

Incentives in the form of payment accepted which generally exceeds patients' expenses incurred by doctor-investigators lead them to enroll inappropriate participants. According to Foster (2003), a doctor may receive $3000 per recruit or higher and a quota of 30 patients may be called for in the study design. A study has shown that there are doctor-investigators who recommend trial drugs to patients by participating in clinical trials although the patients are likely to be better treated with existing treatments or no treatment (Shimm & Spece, 1991). There are also studies showing that doctor-investigators do not care about the inclusion and exclusion criteria established by the research protocol by recruiting patients who had no connection with the illness thus posing a danger to the safety of life of their patients. In fact, there are also doctor-investigators who commit fraud, falsifying recruit records solely to earn more income (Gatter, 2006; Lemmens & Miller, 2003; Caulfield & Griener, 2002).

Furthermore, money can also interfere with the researcher's ability to promote the rights and welfare of human subjects. A doctor-researcher with strong financial or personal interests in recruiting human subjects for a clinical trial may oversell the trial to his patients or take other steps to compromise the informed consent process (Shamoo & Resnik, 2003). The existence of a doctor-patient relationship also indirectly leads the patients to believe and feel confident that the invitation to participate in the trial is for their best interest. In addition, the borne illness makes patients have to rely on doctor-investigators to decide whether to enroll in the trial making them easy prey to be exploited as research subjects. This seems to be true by virtue of Paragraph 26 of the World Medical Association Declaration of Helsinki which states: "When seeking informed consent for participation in a research study the physician should be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such situations the informed consent should be sought by an appropriately qualified individual who is completely independent of this relationship". In fact, it is well established that the doctor-patient relationship is generally one of dependence. This is true in Malaysia. As mentioned earlier, the Malaysian society, especially the patients place great trust on their doctors. As such, doctors do not disclose full information to them. A study by Yuhanif, Anisah & Zaki Morad (2014) revealed that doctor-investigators fail to disclose full information to patients. Instead, doctor-investigators only disclosed information which they thought were necessary for

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the patients to know. The study also showed that there were doctor-investigators who did not disclose information at all to their patients.

In Malaysia, there is no study that has been conducted on conflict of interest of doctor-investigators. However, this does not mean that there is no such problem in the country. In support of this view, a reference can be made to the points put forward by the former Chairman of Malaysian Research Ethics Committees Dato' Dr. Zaki Morad Mohamed Zahir (personal communication, 1 January 2015). He stated that: *"Konflik kepentingan memang wujud di kalangan doktor-penyelidik di Malaysia antaranya adalah melalui bayaran yang diterima daripada pihak industri sebagai balasan merekrut pesakit ... by right doktor-penyelidik kena bagitau pesakit tentang perkara ini tapi banyak orang (doktor-penyelidik) tak bagi tau."* This opinion is also shared by the former Director of Clinical Research Centre Ministry of Health Dr. Lim Teck Onn (2008) in his paper titled, "Case studies and ethical issues in clinical trial" which was presented at the Good Clinical Practice Workshop held by the Sultanah Bahiyah Hospital Alor Setar on the 12 to 14 August 2008. He stated that, *"Conflict of interests is extremely common, in fact conflict of interests is unavoidable"*. Indeed, it is undeniable that the doctor-investigators should be given compensation for their time, expertise and effort to do research. One could argue, however that the incentives in the form of generous payment are intended to do more than merely compensate doctors for their effort (DeRenzo, 2000). As such, money or reward given by drug companies to doctors for recruiting patients into a study or trial is considered unethical practice (College of Physicians and Surgeons of British Columbia, 2009).

1.4 Law Relating to Disclosure of Conflict of Interests

Where conflict of interest cannot be avoided, the usual remedy is disclosure. The Declaration of Helsinki explicitly requires doctors to fully disclose information of all their relevant financial conflict of interest to the patient. Article 26 states that: "In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study". Nevertheless, generally patients are not told that the 'doctor' will be paid by the drug company for entering them into a study (Harper & Reuter, 2009). The absence of federal requirements on doctor-investigators or institutions to disclose financial conflict of interest to patients (Kim et al, 2004) makes things worse. To put it simply, the disclosure of information by doctor-investigators on relevant conflict of interest is not a legal requirement. Therefore, it is not surprising that the Institutional Review Boards (IRBs) do not require doctor-investigators to disclose information on the 'payment transactions' during the informed consent process. In fact, there are IRBs who think it is a private matter between doctor-investigators and sponsors (Roizen, 1988). However, there is a precedent in tort law for suing doctor-investigators or institutions for insufficient disclosure of conflicts (*Moore v. Regents of University of California 793 P.2d 479 (CA, 1990),*

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cert. denied 112 S. Ct. 2967 (1992); Grimes v, Kennedy Krieger 782 A.2d 807 (MD, 2001)). This is because the law of negligence holds doctor-investigators liable for failing short of the customary standard in informing patients or subjects about the potential risks of a particular intervention. It is the duty of the doctor-investigators to provide full information to subjects to get consent.

In Malaysia, until today there is no case law decided by the courts on the conflict of interests. In fact, the only guidelines that are related to clinical trials is the *Malaysian Guidelines for Good Clinical Practice* which also does not outline any provisions relating to the duty of doctors to disclose information on the conflict of interests to patients. This raises concerns to various parties. In fact, concerns to this matter was voiced out by the former Director General of Health Tan Sri Dr Mohd Ismail Merican at the *Ethical Issues in Clinical Research Conference* on 22 December 2005 saying that: "As the benefits offered by health research are becoming obvious, so too are the concerns they raised in terms of the ethical, legal and social issues with regard to the participation of human subjects …". Also, a Malaysian local newspaper, the New Strait Times (2002) has reported that: "Eyeing the expanding market for clinical research in the region, Malaysia is trying to position itself as an ideal place for pharmaceutical majors to conduct clinical trials. But critics worry about weak safeguards and poor enforceability of exiting regulation". So, the only way for patient to know whether doctor-investigators have conflict of interest is to ask the doctor-investigators. Nonetheless, it is impossible for this to happen, in view of the attitude of the Malaysian society where patients put high hope on doctors.

Likewise, there have been efforts or measures taken by the government to enforce guidelines on clinical trials. For example, the Control of Drugs and Cosmetics Regulations 1984 (Revised 2006) states that: "The Director of Pharmaceutical Services may issue written directives or guidelines to any person or group of persons as he thinks necessary for the better carrying out of the provisions of these Regulations and which in particular relate to clinical trials". However, it is important to note that these regulations only exist in the form of directives issued by an administrator. Hence, the regulations are weak and can be disputed in terms of their legal aspects as compared to a legislation or an Act passed by the Parliament or the Legislative Assembly which has to go through a fairly rigorous process. As such, it is a high time to impose a duty on the doctor-investigators to disclose information related to conflict of interest to safeguard the patients' welfare. Henceforth, the authors humbly believe that Malaysia should learn from Singapore and adopt a model to formulate regulations governing clinical trials in the country which could be incorporated under the Medicines Act giving such regulations a force of law. This would allow doctor-investigators to be punished if in case they contravene or fail to comply with the Act (regulations). In Singapore, they have Medicines (Clinical Trials) Regulations which have been incorporated under the Medicines Act (Chapter 176, Sections 18 and 74). For instance, section 20 provides that doctor-investigators are prohibited from having any directly or indirectly financial interest in the trial.

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2. Conclusion

Indeed, incentives to doctor-investigators in return for recruiting patients violate the principle of ethics as doctor-investigators cannot put their personal or financial interests above the interests of patients. However, this is not an easy thing to do because when confronted with generous money then anyone would be influenced. As such, when faced with the problem of conflict of interest, a doctor-investigator must be honest with patients by disclosing related information and recruiting only a qualified patient as the research subject. This is because the doctor-patient relationship which is based on trust and dependency creates an unusually high danger of exploitation and abuse. In fact, doctor-investigators must also be honest with themselves as medical code of ethics clearly prohibits them to put their personal interests above the interests of their patients. This is so because doctor-investigators' financial conflict of interest have the potential to undermine this trust. When there is no trust in the doctor-patient relationship, then there is no guarantee of continuity in the progress of clinical trials as there would be no participation by patients. It is indeed a matter of balancing between these two conflicting interests. Hence, it is inevitable that Malaysia should indeed learn from the Singapore as a model to formulate its own laws dealing with clinical trials.

3. References

Caulfield, T. and Griener, G. 2001. Conflict of interest in clinical research: Addressing the issue of physician remunition. 30(2) *Journal of Law, Medicine & Ethics*, 30(2), p.305.

Gatter, R., 2006. Conflict of interest in International Human drug research and the insufficiency of International protections. *American Journal of Law & Medicine*, 32, p.351- 364.

Roizen, R. 1998. Why I oppose drug company payment of physician/investigators on a per patient/subject basis. *IRB*, 10, p.9-10.

Lemmens, T. & Miller, P.B. 2003. The human subjects trade: Ethical and legal issues surrounding recruitment incentives. *Journal of Law, Medicine & Ethics*, 31, p.398.

Lenrow, D.A. 2006. The treating physician as researcher: Is assuming this dual role a violation of The Nuremberg Code?' *Temple Journal of Science Technology & Envirenmental Law*, 25(1), p.15-48.

Shimm D. S. and Spece R. G. 1991. Industry reimbursement for entering patients into clinical trials: Legal and ethical issues. *Annals of Internal Medicine*. 115(2), p.148-151.

Kim, S.Y.H., Millard, R.W., Nisbet, P., Cox, C. and Caine, E.D. 2004. Potential research participants' views regarding researcher and institutional financial conflicts of interest. *Journal of Medical Ethics*. 30, p.73-79.

Lo, B. Wolfe, L. and Berkekeley, A. 2000. Conflict-of-Interest policies for investigators in clinical trials. *The New England Journal of Medicine*. 343, p.1616-20.

Srinivasan, S. 2010. Patient protection in clinical trials in India: some concerns. *Perspect clinical research*. 1(3), p.101-103.

eISBN 978-967-11473-3-7

Yuhanif Yusof, Anisah Che Ngah and Zaki Morad Mohamad Zaher. 2014. Informed consent in clinical trials with reference to information disclosure to patient-subjects. *Public Health Research*. 4(1), p.384-390.

Foster, R.S. 2003. Conflicts of interest: recognition, disclosure, and management. *J Am Coll Surg*. 196(4), p.505–17.

DeRenzo, E. 2000. Coercion in the recruitment and retention of human research subjects, pharmaceutical industry payments to physician-investigators and the moral courage to the IRB. *IRB*. 22, p.1-5.

Harper, B. and Reuter, S. 2009. Paying Fees to referring physicians: Ethical or Not Ethical?. *Monitor*. p.29-34.

World Medical Assn. 1997. Declaration of Helsinki. *JAMA*. 277, p.925-6.

Shamoo, A. E. and Resnik, D. B., 2003. *Responsible conduct of research*. Oxford University Press.

Smith, V.A., 2008. *Volunteers for medical research are desperately needed*. in Wiener, G. (ed.), At Issue – Volunteerism, Greenhaven Press, Farmington Hills, 2008.

Khushf, G. and Gifford, R., 1998. *Understanding, assessing and managing conflict of interest.* In: McCullough LB, Jones JW, Brody BA, eds. Surgical ethics. New York: Oxford University Press.

WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects <www.wma.net/en/30publications/10policies/b3 [Assessed 12 June 2014].

Zaki Morad Mohamed Zaher., 2014. *Interview on conflict of interests*. Interviewed by Yuhanif Yusof [tape recorder] 1 January 2015, 04:30.

Lim Teck Onn, 2008. Case studies and ethical issues in clinical trial. CRC Hospital Sultanah Bahiyah, *Good Clinical Practice Workshop*. Hospital Sultanah Bahiyah Alor Star, 12-14 August 2008. Kedah: Malaysia.

Ismail Merican, 2005. Message from the Director General of Health Malaysia. Institute of Medical Research, *Ethical Issues in Clinical Research Conference*. Institute of Medical Research, 22 December 2005. Kuala Lumpur: Malaysia.